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Maier, Larissa J ; Haug, Severin ; Schaub, Michael P

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ORIGINAL ARTICLE

Prevalence of and motives for pharmacological neuroenhancement in Switzerland–results from a national Internet panel

Larissa J. Maier[a], Severin Haug[a], Michael P. Schaub[a]

[a] Swiss Research Institute for Public Health and Addiction (ISGF), Associated Institute at the University of Zurich and WHO Collaborating Centre, Zurich, Switzerland

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Corresponding author

Dr. Des. Larissa J. Maier, Swiss Research Institute for Public Health and Addiction (ISGF), Associated Institute at the University of Zurich, Konradstrasse 32, Postfach, Zurich, CH-8031, Switzerland.

Phone: +41 44 448 11 73. Fax: +41 448 11 70. Email: larissa.maier@isgf.uzh.ch

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Abstract

Aims To estimate the prevalence of self-reported pharmacological neuroenhancement (PNE) with prescription or recreational drugs among the Swiss general population and correlates of PNE. **Design** A population-based cross-sectional study using a self-administered online survey. **Setting** A telephone-recruited highly representative Internet Panel in Switzerland. **Participants** A total of 10 171 Swiss employees and students (unweighted *N* = 10 084) aged 15 to 74 years (mean age: 39.1 ± 13.3; 46.6% female). **Measurements** Self-reported lifetime, past-year, and past-month use of prescription or recreational drugs for PNE, motives for use, and correlates of PNE including socio-demographic, health, and recreational drug use characteristics. **Findings** The lifetime prevalence of PNE was 4.0% (95% CI = 3.62, 4.38), and the past-year prevalence was 2.1% (95% CI = 1.82, 2.38). Lifetime pharmacological mood enhancement (3.1%; 95% CI = 2.76, 3.44) was more prevalent than pharmacological cognitive enhancement (1.4%; 95% CI = 1.17, 1.63). Fifty-four participants reported both (0.5%; 95% CI = 0.36, 0.64). PNE was associated with studying rather than full-time (OR = 0.35; 95% CI = 0.21, 0.57) or part-time employment (OR = 0.39; 95% CI = 0.23, 0.67), stress (OR = 1.51 95% CI = 1.31, 1.75), cocaine (OR = 2.40; 95% CI = 1.51, 3.82) and amphetamine use (OR = 2.44; CI 95% = 1.37, 4.33), diagnosis of a mental disorder (OR = 4.26; 95% CI = 3.14, 5.80), and perceived poor health (OR = 0.76; 95% CI = 0.64, 0.90). **Conclusions** Pharmacological neuroenhancement was rare among Swiss employees and students (4.0%). Pharmacological mood enhancement (3.1%) is more prevalent than direct cognitive enhancement (1.4%).

Key reference terms

Pharmacological neuroenhancement; cognitive enhancement; mood enhancement; nonmedical prescription drug use; illegal drug use

Introduction

The use of prescription or recreational drugs by healthy individuals to enhance cognitive or affective function [1,2] is termed pharmacological neuroenhancement (PNE) when explicitly used for the purpose of improved performance at work or in education [3]. Prescription drugs indicated for the treatment of psychiatric disorders such as attention-deficit hyperactivity disorder (ADD/ADHD) or narcolepsy are the focus of the PNE debate because these drugs also have cognitive-enhancing effects in healthy individuals [1,4].

The prevalence of nonmedical stimulant use is well researched among American college students although differentiation of motives for use is often lacking [5–9]. While the estimated annual prevalence of drug use for PNE was 4.0% [10], estimated nonmedical use ranged from 1.5% to 35% [11,12]. The most recent and most comprehensive review estimated the rate of prescription stimulant misuse among college students at 17.0% [13]. Table 1 provides an overview of recently published studies estimating specifically the prevalence of PNE among different study samples and different substances used to improve performance at work or while studying.

(Table 1)

Several recent studies have concluded that the use of psychoactive substances for cognitive enhancement among students is less prevalent in Europe than in the United States [3,14–17]. Three Swiss studies have addressed the prevalence of PNE among students and young Swiss men and reported a lifetime prevalence of PNE of 3.0% to 13.8% but only rare current regular use [18–20]. The highest prevalence rate was, however, due to the inclusion of the recreational drugs alcohol and cannabis, which were not only used recreationally (90.2% and 43.3%, respectively) but also to improve study performance (5.6% and 2.5%, respectively) [20]. Swiss students reported the use of illegal stimulant mainly for recreation (MDMA= 5.2%, cocaine = 4.2%, and amphetamine = 3.7%) and rarely to enhance study performance (all < 0.5%) [20] Consistent with previous research [9], all of the Swiss studies observed a positive association between recreational drug use and PNE [18–20]. However, the study estimating the prevalence of PNE among young Swiss men is not included in Table 1 because of a lacking predefinition of the purpose of illicit drug use [19].Despite an increasing number of research publications on PNE, the generalizability of the research results is problematic because the inclusion of substances used for PNE differs greatly among studies [3,21]. Furthermore, the distinction between medical use and nonmedical use is often not clear. In general, the 12-month prevalence of prescription stimulant use in the Swiss population is low (0.5%) and most prevalent among youth and young adults [22]. Past-year use of sedative

prescription drugs is more prevalent (9.7%) and associated with female gender and increased age [22]. Although the source of supply was specified, nonmedical use was not further specified.

Interpreting the results for the prevalence of PNE is also complicated by differences among countries in the approval of medication for the treatment of mental health disorders. Moreover, users are often not aware of the trade names of prescription drugs, and this lack of awareness may bias the outcome of the prevalence of prescription drug use in surveys. A substantial advantage of online surveys is the presentation of pictures of putatively enhancing drugs to facilitate the recognition of the drugs that have been used [23]. The present study is the first in Europe on the topic of PNE to combine questions about the prevalence of the use of prescription and over-the-counter drugs with pictures of the pills, blister, and packaging. In addition, previous studies of the prevalence of and attitudes toward PNE have focused primarily on vulnerable groups, such as students [5,8,16,24], scientists [25], physicians [26], and pilots [27,28], but never on the general population.

This study was designed 1) to estimate the prevalence of PNE among employees and students in Switzerland considering different motives for use; 2) to identify relevant substances used for direct cognitive enhancement (PCE) or increased psychological well-being and mood enhancement (PME); and 3) to investigate the differences between people experienced with PNE and non-users to reveal potential predictors for PNE.

Materials and methods

Participants and enrollment procedure

Participants were drawn from a representative Internet panel of the LINK institute for market and social research in Switzerland, which consists of more than 130 000 people living in Switzerland who consented to be contacted for public opinion surveys administered through the Internet. The LINK institute uses a computer-assisted telephone interviewing system to recruit panelists representing the Swiss general public. These panelists are representative of the 15- to 74-year-old population of Switzerland that uses the Internet at least once per week for private purposes and is able to answer a questionnaire in German, French, or Italian. The study was conducted during March 2013, and participants were rewarded with one of the following incentives, equal to a value of approximately 2 Euros: points for supermarkets, bookshops, or donation campaigns.

A total of 39 996 e-mail invitations were sent out, and 18 094 began the survey, corresponding to approximately 45.2% of the invitations. Of the 18 094 panelists who responded, 12 404 met the eligibility criteria (currently employed or in education and quota not yet fulfilled) for the study. A total of 10 084 (82.3%) completed the survey; 2320 (18.7%) did not complete the survey (see participant flow diagram; Fig. 1).

(Fig. 1)

The self-reported data on PNE and correlates were weighted for age, gender, and language region to create national-level estimates of the prevalence of neuroenhancement. The definition of quota cells for the sample was based on the data for the constant resident population of Switzerland (STATPOP) published by the Federal Statistical Office. Informed consent was obtained from all participants included in the study. The final weighted sample referred to in the present paper consisted of 10 171 participants; the number of interviews realized per quota cell and the resulting weighting factor for the data for each language region in Switzerland are provided in the supplementary materials (Table S1).

Outcome measures

A self-administered online questionnaire based on previous surveys of substance use at work or while studying was used to estimate the prevalence of PNE as well as important correlates such as socio-demographic data, stress, and physical and mental health; the specifications of the questionnaire design are provided in the supplementary materials (Methods S1). The questionnaire was pretested with 103 participants of the LINK Internet panel and improved accordingly.

Participants were asked whether they were aware of PNE and whether they knew other people using prescription or recreational drugs intentionally to enhance cognition or mood at work or while studying. The prevalence of and the two main motives for PNE at work or for studying were examined through two principal questions. First, participants were asked whether they had ever used prescription or recreational drugs to enhance their cognitive performance at work or while studying. Second, they were asked whether they had ever used prescription or recreational drugs to enhance their mood at work or while studying. The group of people who answered affirmatively to at least one of these two questions will be referred to as PNE users hereafter. Cognitive and mood enhancement were the two main motives of interest, but all participants were required to indicate for each substance used whether the use was aimed at specific neuroenhancement purposes: to enhance concentration, alertness, and vigilance; to reduce nervousness; to enhance mood at work or while studying; and to relax after stress at work or in education.

Statistical analysis

Descriptive statistics provided information about the prevalence and substances used for PNE; the prevalence of the use of alcohol, illegal drugs, and legally available soft enhancers; the frequency of stress; and the physical

and mental health states of the participants. Initially, we performed separate logistic regression analyses (subsequently termed 'univariate analyses') to evaluate the ability of each independent variable to predict the lifetime use of PNE. All predictors from the univariate analyses were entered into a fully adjusted multivariable model. Nagelkerke's R-square was calculated as a goodness-of-fit measure for the multivariable model. All quantitative analyses were conducted using IBM SPSS Statistics Version 22 (SPSS Inc., Chicago, IL, USA). Significance was set at $P < 0.050$.

Results

Participant characteristics

The stratified sample displayed an equal distribution of gender (46.5% female) and a mean age of 39.1 years (*SD* = 13.3). The majority of participants were German-speaking and worked full- or part-time. Three of four participants (71.6%) were aware of PNE. One-quarter of the sample was aware of one (14.3%) or more (11.5%) people in their circle of acquaintances who had used prescription or recreational drugs at least once to enhance their cognitive performance (PCE) at work or while studying. One fifth of the participants, however, knew one (11.6%) or more (8.2%) people who had used psychoactive substances to increase psychological well-being (PME) at work or while studying. Participants who knew at least one PNE user (35.0%) were seven times more likely to report own experiences of PNE (OR = 7.03; 95% CI 5.55, 8.90). Moreover, a small number of participants reported that their friends had already recommended PCE (4.3%) or PME (2.3%) to them. A narrow majority of the sample did not recognize any justification for PNE (57.7%), and only a few people were willing to use prescription drugs (8.7%) or recreational drugs (4.0%) to improve their performance at work or while studying, even if the hypothetical case that the drugs were effective was true. Furthermore, the majority of the participants believed that the use of prescription and recreational drugs for PNE might be harmful (74.3% and 85.3%, respectively).

Prevalence of PNE

The participant characteristics for the analysis of lifetime PNE are presented in Table 2. Of the study participants, 4.0% (n = 411; 95% CI = 3.62, 4.38) reported the use of prescription or recreational drugs to perform better at work or while studying (PNE). Lifetime PME to perform better at work or while studying (3.1%; 95% CI = 2.76, 3.44) was more prevalent than PCE (1.4%; 95% CI = 1.17, 1.63) Fifty-four participants reported both (0.5%; 95% CI = 0.36, 0.64). The past-year prevalence of PNE was 2.1% (n = 215; 95% CI = 1.82, 2.38).

Univariate predictors of lifetime PNE

As shown in Table 2, all variables were univariate predictors of lifetime PNE.

(Table 2)

The lifetime use of recreational drugs and soft enhancers as univariate predictors for PNE is displayed in Table 3. The lifetime use of tobacco, illegal drugs, and over-the-counter (OTC) drugs was more prevalent among PNE users. No association was observed for lifetime use of alcohol and caffeine products. Only a few people reported the use of a fictitious drug; these individuals were, for the most part, not experienced with PNE (Table 3).

(Table 3)

Multivariable predictors of lifetime PNE

The overall prediction model resulting from a hierarchical logistic regression (R^2 = 0.27) is presented in Table 4 and revealed that the following variables were positively associated with lifetime PNE: being a student, frequent stress in the past 12 months, psychological consulting, lifetime diagnosis of a mental disorder, and lifetime use of cocaine and illegal amphetamine. Having minor children at home and perceived health were negatively associated with lifetime PNE.

(Table 4)

Prescription drugs used for PNE, motives for use, and source of supply

Tranquilizers and antidepressants were the substances most commonly misused, and current prescription drug misuse within the past 30 days was rare for all prescription drug categories (Table 5). Among PNE users, 26.2% reported lifetime nonmedical use of tranquillizers, 20.2% antidepressants, 14.2% ADD/ADHD medication, 3.5% beta-blockers, 1.8% modafinil, and 0.4% anti-dementia drugs. The prevalence of nonmedical use of each medication evaluated in the survey is available in the supplementary materials (Table S2). The source of supply for the nonmedical use of prescription drugs was most commonly a doctor (Table 5). However, the main source of supply for ADD/ADHD medication was friends (Table 5). A narrow majority of the PNE users reported the desired effects of PNE with prescription drugs (Table 5).

(Table 5)

The reported nonmedical use of tranquilizers was aimed mainly at improving sleep and relaxation after stress at work or in education (33.5%). The main motive for the nonmedical use of antidepressants was PME at work or while studying (58.8%) as well as PME in leisure (38.3%). ADHD medications were most commonly misused for PCE (74.5%). The only two people who mentioned the misuse of an anti-dementia drug both used the drug for the purpose of PCE. The number of participants who used modafinil and beta-blockers without having a prescription or other than prescribed was too small to make reliable statements about the motives for use.

Recreational drugs used for PNE, motives for use, and source of supply

Alcohol users mentioned relaxation during leisure time as their most important motive for drinking alcohol. Partying and getting high were the main motives for the use of illegal drugs (87.4% for MDMA, 77.7% for cocaine, 73.2% for illegal amphetamine, 59.2% for ketamine, 54.7% for cannabis) except for GHB/GBL, for which half of the self-named users reported that their use occurred involuntarily. However, 15.2% of illegal amphetamine and 11.6% of cocaine users reported that they had already used these drugs intentionally for PCE (Table 5). Moreover, the use of alcohol and cannabis to relax and to calm down after stress in the workplace or education, which would be considered indirect PNE [3], was reported by one quarter of alcohol users and one fifth of cannabis users (Table 6).

(Table 6)

The main source of supply for illegal drugs was the circle of friends (91.3% for cannabis, 80.8% for MDMA, 78.7% for illegal amphetamine, 78.0% for cocaine, 69.3% for ketamine, 57.7% for GHB/GBL) and, less commonly, a dealer (41.9% for GHB/GBL, 33.7% for ketamine, 32.9% for MDMA, 29.1% for cocaine, 27.6% for illegal amphetamine, 14.6% for cannabis). Only a minority of users had bought their drugs on the Internet (15.9% for ketamine, 5.9% for GHB/GBL, 2.0% for illegal amphetamine, 0.9% for cocaine, 0.7% for MDMA, 0.5% for cannabis) or received them from family members (9.4% for ketamine, 5.2% for GHB/GBL, 3.0% for cannabis, 2.1% for illegal amphetamine, 2.2% for cocaine, 1.1% for MDMA).

Discussion

This study is the first representative large-scale study of PNE among the Swiss population that did not focus solely on students but also on employees and surveyed the various substances used for PNE. The study revealed three main findings. 1) Among the study sample, 4.0% reported lifetime use of prescription or recreational drugs for PNE, but only half of these respondents (2.1%) reported PNE within the past year. 2) Lifetime diagnosis of a mental disorder, experience with professional psychological consulting, stress, being a student, living without minor children at home, perceived poor health, and the lifetime use of the illegal stimulants cocaine and amphetamine were the strongest predictors of lifetime PNE. 3) PME was more prevalent than PCE or both PME/PCE.

According to our study, the lifetime and 12-month prevalence rates of PNE were rather low compared to other studies (see Table 1) or general prescription and recreational drug in the Swiss population [22,29]. This result is consistent with recent research on substance use for PNE among German and Swiss employees [30–32] but indicates a lower prevalence compared to Swiss student-only surveys [18,20]. The willingness to use prescription drugs or recreational drugs for PNE for the hypothetical case that they were effective without any side effects was considerably low among study participants without self-reported PNE (8.7% and 4.0%, respectively). However, the interest in PNE was slightly higher among students, demonstrating the need to monitor PNE among youth in Europe. The authors of a recent study of PNE among UK students claimed that the low prevalence despite high interest might be explained by the lack of availability of prescription drugs [33].

Participants who reported a lifetime diagnosis of a mental disorder were more than four times more likely to report PNE. Moreover, participants who felt often or very often stressed during the past 12 months and participants who rated their health as only poor were also more likely to report PNE. Having minor children at home was found to be a protective factor that made the occurrence of PNE unlikely. The association between illegal drug use and PNE established in the literature [6,9,20,34] was confirmed in the present study. Participants who reported having used cocaine or illegal amphetamine were more than two times more likely to report PNE.

The nonmedical use of antidepressants and tranquilizers for increased well-being (PME) was more prevalent than stimulant use for cognitive enhancement. Furthermore, the majority of PME users had previously sought help because of a mental health problem and were assumed to misuse their current or past medication for PNE [7,35]. The finding that the participants reported greater awareness of PCE by others (25.8%) compared to PME by others (19.8%), although opposite prevalence rates of substance use for these purposes were reported, potentially indicating underreporting of PCE in the present study. In addition, the use of sedating substances, such as alcohol and cannabis, to relax after stress in the workplace or education was more common than illicit stimulant use for PCE and can be viewed as a form of indirect PCE if used to increase relaxation to perform

better the next day [3]. The frequent and high use of alcohol (and/or cannabis) as a socially accepted strategy to cope with stress may cause greater harm than occasional PCE with prescription drugs during short periods in life. However, further studies are needed to determine if PCE use by students continues after graduation.

Strengths, limitations and implications

A major strength of this study is the large sample of employees and students recruited as part of the Swiss national Internet panel of the LINK institute, which is representative of the Swiss population. Furthermore, thorough weighting procedures were used to investigate substance use for the purpose of cognitive and mood enhancement at work or while studying. Moreover, this survey included authentic photos of each medication to facilitate user recognition and inquired specifically about nonmedical use and its motives. In addition, two fictitious drugs were included to control for socially desirable responding behavior.

However, the ability of the Internet panel to provide representative data may be questioned. Do only middle-class Swiss people with good jobs and a good social context participate in these surveys? Could PNE be underestimated in Switzerland because the stressed population who requires enhancement does not have time to occasionally participate in surveys for an Internet panel? What type of student is likely to engage in an additional Internet panel for surveys if already flooded with invitations to participate in research studies at their higher education institution?

A further limitation is the formulation of the question about PNE. The two main questions asked about participants' use of prescription and recreational drugs to perform better at work or while studying. Most of the participants had most likely not considered indirect enhancement with sedating substances for PNE when responding to questions about substance use for performance. Therefore, a more specific definition of PNE should be implemented in subsequent surveys [3]. In addition, we asked about a broad range of potential prescription drugs used for PNE (Table S2) but did not address the issue of generic medication.

The identification of two different types of PNE users with different motives for substance use has several implications for preventing physical and mental harm. First, healthy PNE users without a current or past mental disorder should be informed about the possible risks and side effects of PNE use. Academic institutions and companies could provide students and employees with information about strategies other than substance use and develop stress-management training as tools for early prevention of PNE in healthy individuals. Moreover, increased communication about the addiction potential of certain drugs used for PNE is needed, and doctors should be able to furnish objective information about the effects, side effects, and individual differences in response to prescription drugs. Second, PNE users with an underlying mental disorder who receive no or only

insufficient treatment should be informed about further treatment options. Corporate interventions must be implemented if the mental disorder is associated with the workplace situation and job changeover is not desired. Third, workplace health promotion should address the issue of stress and successful coping strategies before PNE occurs. This goal could be achieved by strengthening the social and communication skills of the employees and management. Finally, future research should investigate differences between PNE users with and without a current or past mental disorder. The motives and profiles of "healthy" and more vulnerable PNE users likely differ and consequently require different intervention measures.

Conclusions

Our research constitutes the first comprehensive and representative large-scale study of PNE on a national level in Europe. Among the Swiss population, 4.0% reported lifetime PNE, but only 2.1% reported past-year PNE. Lifetime PNE was strongly associated with prior diagnosis of at least one mental disorder, with being a student rather than employed, and with illegal stimulant use experience. PNE is not (yet) common among the Swiss population, but monitoring further development is recommended.

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Conflicts of interest

The authors have no financial disclosures and no competitive interests. The study funders (SUVA) did not influence the design and conduct of the study; the collection, management, analysis, or interpretation of the data; or the preparation, review, or approval of the manuscript.

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Table 1 Studies estimating the prevalence of pharmacological neuroenhancement (PNE) published between 2000 and 2015; only PNE specific studies are included in the table. Please refer to Benson et al. [13] for a general overview of studies estimating the prevalence of nonmedical prescription stimulant misuse.

Author (Year)	*Study sample*	*Lifetime prevalence of PNE*		*12-month prevalence of PNE (or other if specified)*		*Prevalence soft enhancement*
		Prescription drugs (nonmedical use)	*Recreational drugs (for enhancement)*	*Prescription drugs (nonmedical use)*	*Recreational drugs (for enhancement)*	*Caffeine, food supplements, OTC-drugs*
Arria et al. (2013) [36]	984 U.S. college students	38.0% stimulants to help study at least once in 4 years				
Castaldi et al. (2012) [14]	77 Italian university students (limitation: unclear whether OTC drugs are included)	16.0% – drugs to improve attention, cognitive performance or memory or to cope with fatigue and sleepiness				
DAK (2009) [30]	3017 German employees aged 20 to 50 years old	1.0% to 5.0% MPH, MOD, ATD, BB, or ADEM to improve performance at work		2.2% regular users		
DAK (2015) [32]	5017 German employees aged 20 to 50 years old	6.7% MPH, MOD, ATD, BB, or ADEM to improve performance at work 3.3% cognition 4.7% mood and reduced nervousness		4.2% regular users 3.2% – all 1.5% cognition 2.1% mood and reduced nervousness		
DeSantis et al. (2008) [7]	1811 U.S. college students	23.2% stimulants to stay awake to study 21.5% stimulants to concentrate on your work 11.8% stimulants to help memorize Any purpose:				

		34.0% stimulants				
Dietz et al. (2013) [37]	2569 German university students			20.0% – all (RRT) [a]		
Eickenhorst et al. (2012) [15]	1218 German university students and 106 German graduates	7.0% illicit drugs – MPH, MOD, DEX, ATD, BB, COC, HER, or MDMA				*Lifetime* 89.3% COF [c] 25.2% HSED 11.1% CAFT
Forlini et al. (2014) [38]	1026 German university students	2.2% – drugs to enhance attention, endurance, and cognitive function	3.8% CAN 1.4% AMPH 1.3% COC 1.0% MDMA			*Lifetime* 55.9% COF 40.8% ED
Franke et al. (2011) [16,39]	1035 German high school and 512 German undergraduate university students	1.3% stimulants – all	2.6% illegal stimulants	0.3% stimulants – all < 0.1% – all (*30 d*)	1.0% illegal stimulants 0.3% – all (*30 d*)	*Lifetime/12 m/30 d* 53.2%/8.5%/6.3% COF 39.0%/10.7%/6.3% ED 10.5%/3.8%/0.8% CAFT
Franke et al. (2013) [40]	1145 German surgeons	8.9% illicit drugs – all (vs. 19.9% RRT) 2.6% DEX 2.5% MPH 2.2% MOD 2.4% ATD (vs. 15.1% RRT) 1.6% COC 1.2% EPH 0.9% AMPH 0.6% MDMA 0.6% ATX 0.3% ADEM		3.0% illicit drugs – all 1.4% illicit drugs – all (*30 d*) 0.8% illicit drugs – all (*7 d*) 1.0% ATD 0.5% ATD (*30 d*) 0.4% ATD (*7 d*)		
Franke et al. (2014)	3306 surgeons at international conferences					*Lifetime/12 m* 66.8%/61.9% COF 24.2%/15.4% ED 12.6%/5.9% CAFT *30 d/7 d* 56.9%/50.5% COF 9.9%/6.1% ED

						4.7%/3.8% CAFT
Gay et al. (2007) [41]	663 French employees	24.1% – all	7.5% ALC 2.1% CAN			*Lifetime* 10.3% NIC
Grebner et al. (2010) [31]	1004 Swiss employees			4.0% drugs to improve cognitive performance or mood at work 10.0% drugs to relax or sleep after stress at work (to work better the next day)		
Mache et al. (2012) [42]	1053 German university students	1.0–13.0% illicit drugs – all 15.0% CAN [b] 2.3% COC 2.2% MPH 2.0% BB 1.0% MOD 1.0% FLX 0.1% PIR				*Lifetime* 22.0% HSED 10.0% CAFT
Maher et al. (2008) [25]	1427 academics from 60 countries	20.0% – all 12.4% MPH 8.8% MOD 6.0% DEX & other 3.0% BB				
Maier et al. (2013) [20]	6275 Swiss university students	7.8% – all 4.1% MPH 2.7% SED/SLP 1.2% BB 0.5% ATD 0.3% MOD 0.1% ADEM	7.6% – all 5.6% ALC 2.5% CAN 0.4% AMPH 0.2% COC 0.1% MDMA 0% GHB/GBL	*30 d prior to last exam* 2.6% MPH 2.1% SED/SLP 0.7% BB 0.4% ATD 0.2% MOD 0.1% ADEM	*30 d prior to last exam* 5.1% ALC 1.8% CAN 0.3% AMPH 0.1% COC 0.02% MDMA 0% GHB/GBL	*Lifetime/30 d prior to last exam* 53.2%/49.1% COF 35.9%/29.7% ED 18.2%/14.9% VT 18.2%/13.2% HSED 4.4%/2.6% CAFT
Mazanov et al. (2013) [43]	1729 Australian university students	1.9% MOD/RAC to study 4.4% MPH/DEX to study 1.5% SED to study	4.5% illegal drugs to study			*Lifetime/* 63.5% CAF 22.0% OTC
McNeil et al. (2011) [44]	243 U.S. dental & dental hygiene	8.2% stimulants to improve attention/				

	students	concentration 1.6% stimulants for higher grades DEX > MPH			
Middendorff et al. (2012) [45]	7989 German university students	5.3% illicit drugs – all 1.3% various drugs 1.2% CAN 1.0% MPH 0.6% BB 0.5% AMPH 0.2% MOD 0.2% COC 0.1% MDMA			*Lifetime* 5.2% – all [d] 4.3% HSED [d] 0.8% CAF [d]
Ott & Biller-Andorno (2014) [18]	1765 Swiss university students	4.7% ADHD drugs to help study MPH < MOD < DEX			
Partridge et al. (2012) [46]	1265 Australian university students	2.4% drugs to enhance concentration and alertness			
Prudhomme White et al. (2010) [47]	1025 U.S. university students	8.7% MPH to improve study habits 3.2% MPH to improve grades Any purpose: 16.2% stimulants			
Rosiers & Van Hal (2005) [17]	1501 Flemish university and college students			2.9% stimulants 2.6% stimulants (*exams*)	
Sattler & Wiegel (2013) [48]	5882 German university students	4.6% drugs to enhance the cognitive efficiency		3.2% – all 2.3% – all (*6 m*) 1.2% – all (*30 d*)	
Schelle et al. (2015) [49]	1572 Dutch university students	1.7% drugs to improve cognitive function	1.3% illegal drugs 1.8% ALC [e]		*Lifetime* 45.6% – all [e] 41.7% CAF 9.0% OTC

						3.0% NIC 0.5% SMA [f]
Schilling et al. (2012) [50]	6142 German participants (any)				1.5% illicit drugs – all 1.2% ATD 0.5% AMPH 0.1% BB	
Singh et al. (2014) [33]	877 UK university students	6.2% MOD 4.0% MPH 2.0% ADD				*Lifetime* 24.3% CAFT
Teter et al. (2006) [51]	4580 U.S. college students	5.4% stimulants to concentrate 5.0% stimulants to study 4.0% stimulants to increase alertness DEX > MPH Any purpose: 8.3% stimulants		Any purpose: 5.9% stimulants – all 4.5% DEX 1.4% MPH		
Timmer et al. (2012) [52]	422 Dutch psychiatrists and doctors working in psychiatry			11.0% – all 5.0% BZD 4.0% BB 2.0% MPH		
Wolff et al. (2014) [53]	1007 German university students	5.8% – drugs to increase cognitive performance	3.5% illegal drugs	3.0% – all	1.7% illegal drugs	*Lifetime/12 m* 83.2%/52.3% – all

[a] Including not only prescription and recreational drugs but also caffeine tablets and should, therefore, be interpreted carefully. [b] The study authors report themselves a prevalence of illicit drug use for PNE of 1.0-13.0% but cannabis use for PNE was reported by 15.0% of participants [42]. [c] Students reported also the use of the lifestyle drugs, alcohol (83.0%), nicotine (33.0%), and cannabis (14.0%) during their studies, which is not reported in the table, because it refers not to PNE use. [d] Post-coded ("other") and, therefore, underestimated. [e] Alcohol was categorized as lifestyle drug together with nicotine and legally available OTC drugs similar to the category soft enhancement here. However, alcohol is not considered "soft" because the effects and consequences can be compared with those of illegal drugs that are used recreationally. [f] Legal available psychoactive substances that are sold in Smart shops. ADEM: anti-dementia drugs; ADHD: attention-deficit hyperactivity disorder; ALC: alcohol; AMPH: illegal amphetamine; ATD: antidepressants; ATX: atomoxetine; BB: beta-blockers; BZD: benzodiazepines; CAF: products containing caffeine; CAFT: caffeine tablets; CAN: cannabis; COC: cocaine; COF: coffee; DEX: dexamphetamine; ED: energy drinks; EPH: ephedrine; FLX: fluoxetin; GHB/GBL: gamma-hydroxybutyrate/gamma-butyrolactone; HER: heroine; HSED: herbal sedatives; MDMA: 3-4 methylenedioxymethamphetamine (ecstasy); METH: methamphetamine; MOD: modafinil; MPH: methylphenidate; NIC: nicotine; OTC: over-the-counter drugs; PIR: piracetam; RRT: randomized response technique; SED: sedative medication; SLP: sleeping pills; SMA: legal available products from smart shops; VT: vitamins and tonics.

Table 2 Participant characteristics of the study population with and without experience with PNE and the odds ratios (OR) for the univariate associations of each variable with lifetime PNE.

	Total *N = 10 171*	*PNE* *n = 411*	*No PNE* *n = 9760*	*OR (95% CI)* [a]	*P* [a]
Sex					
Male	53.4% (5433)	3.7% (202)	96.3% (5231)		
Female	46.6% (4738)	4.4% (208)	95.6% (4529)	1.22 (1.00, 1.50)	< .05
Age group					
15–24 years	18.4% (1876)	5.5% (104)	94.5% (1772)		
25–34 years	21.1% (2144)	4.1% (88)	95.9% (2056)	0.73 (0.53, 0.99)	.04
35–44 years	22.1% (2251)	3.9% (87)	96.1% (2164)	0.68 (0.50, 0.92)	.01
45–74 years	38.3% (3899)	3.4% (132)	96.6% (3767)	0.58 (0.44, 0.77)	< .01
Linguistic region					
German	73.3% (7456)	3.8% (285)	96.2% (7171)		
French	22.6% (2302)	5.0% (115)	95.0% (2187)	1.36 (1.09, 1.71)	< .01
Italian	4.0% (412)	2.4% (10)	97.6% (402)	0.61 (0.32, 1.15)	.13
Professional activity					
In education	13.5% (1375)	6.8% (93)	93.2% (1282)		
Full-time work ≥ 90%	54.6% (5553)	3.3% (182)	96.7% (5371)	0.45 (0.35, 0.60)	< .01
Part-time work < 90%	31.9% (3243)	4.2% (135)	95.8% (3107)	0.59 (0.45, 0.79)	< .01
Monthly income [b]					
< 6000 CHF	25.2% (2025)	6.0% (122)	94.0% (1903)		
6000-10 000 CHF	44.2% (3547)	3.3% (117)	96.7% (3430)	0.54 (0.42, 0.71)	< .01
> 10 000 CHF	30.6% (2454)	3.6% (89)	96.4% (2366)	0.58 (0.43, 0.77)	< .01
Relationship					
None/temporary	27.4% (2788)	5.5% (152)	94.5% (2636)		
Stable	72.6% (7383)	3.5% (259)	96.5% (7124)	0.61 (0.50, 0.75)	< .01
Children at home < 18					
None	64.2% (6534)	4.6% (299)	95.4% (6235)		
At least one	35.8% (3636)	3.1% (111)	96.9% (3525)	0.67 (0.54, 0.84)	< .01
Perceived health					
SF-12, scale 1–5	3.49 (0.79)	3.04 (0.87)	3.50 (0.79)	0.46 (0.40, 0.52)	< .01
Stress (12 m)					
SECO, scale 1–5	3.22 (0.94)	3.81 (0.95)	3.20 (0.93)	2.06 (1.84, 2.31)	< .01
Psychological consulting					
Never	79.6% (8091)	1.9% (156)	98.1% (7935)		
At least once	20.4% (2080)	12.3% (255)	87.7% (1825)	7.36 (6.00, 9.08)	< .01
Mental disorder [c]					
Never	78.4% (7970)	1.5% (118)	98.5% (7852)		
At least one	21.6% (2201)	13.3% (293)	86.7% (1908)	10.26 (8.20, 12.83)	< .01

Data are % (number) or mean (standard deviation) adjusted for age, gender, and language region. [a] Population-based weights were removed in the regression analyses. [b] No information provided by n = 2144, all other variables complete. [c] ADD/ADHD, narcolepsy, depression, anxiety disorder, dependency (lifetime diagnosis). PNE: pharmacological neuroenhancement; SF-12: The 12-Item Short Form Health Survey; SECO: State Secretariat for Economic Affairs.

Table 3 Lifetime use of legal and illegal drugs and potential soft enhancers in the sample and the odds ratios (OR) for the univariate associations of substance use with lifetime PNE.

	Total *N = 10 171*	*PNE* *n = 411*	*No PNE* *n = 9 760*	*OR (95% CI)* [a]	*P* [a]
Lifetime drug use					
Alcohol	93.8% (9541)	95.0% (390)	93.8% (9151)	1.30 (0.82, 2.09)	.26
Tobacco	63.2% (6424)	76.2% (313)	62.6% (6111)	1.86 (1.47, 2.36)	< .01
Cannabis	32.1% (3261)	51.5% (211)	31.2% (3050)	2.36 (1.93, 2.89)	< .01
Cocaine	3.7% (378)	17.6% (72)	3.1% (306)	6.65 (5.02, 8.82)	< .01
MDMA (ecstasy)	2.7% (274)	12.8% (52)	2.3% (221)	6.44 (4.65, 8.92)	< .01
Illegal amphetamine	2.0% (207)	12.5% (52)	1.6% (155)	8.77 (6.25, 12.32)	< .01
GHB/GBL	0.6% (60)	3.2% (13)	0.5% (46)	6.83 (3.58, 13.04)	< .01
Ketamine	0.2% (21)	2.4% (10)	0.1% (11)	20.40 (8.41, 49.53)	< .01
Caffeine products [b]	92.8% (9439)	93.2% (383)	92.8% (9057)	1.04 (0.70, 1.55)	.86
Vitamins & OTC drugs [c]	46.0% (4673)	63.4% (260)	45.2% (4413)	2.16 (1.75, 2.67)	< .01
Fictitious drugs [d]	0.2% (25)	1.0% (4)	0.2% (21)	3.51 (1.04, 11.80)	.04

Data are % (number) adjusted for age, gender, and language region. [a] Population-based weights were removed in the regression analyses. [b] Coffee, caffeine tablets, and energy drinks. [c] Herbal sedatives, vitamins, and tonics. [d] Supraval® and Energyl®. PNE: pharmacological neuroenhancement; OTC: over-the-counter.

Table 4 Odds ratios (OR) for the overall model of the multivariable associations (fully adjusted results) between participant characteristics and lifetime PNE.

	OR (95% CI)	*P*
Sex		
Male	0.78 (0.59, 1.03)	.08
Female		
Age group		
15-24 years		
25-34 years	1.14 (0.69, 1.89)	.60
35-44 years	1.33 (0.77, 2.30)	.31
45-74 years	0.88 (0.52, 1.47)	.62
Professional activity		
In education		
Full-time work ≥ 90%	0.35 (0.21, 0.57)	< .01
Part-time work < 90%	0.39 (0.23, 0.67)	< .01
Monthly income [a]		
< 6,000 CHF		
6,000-10,000 CHF	0.90 (0.66, 1.22)	.50
> 10,000 CHF	1.11 (0.79, 1.57)	.54
Relationship		
None/temporary		
Stable	1.02 (0.77, 1.37)	.87
Children at home < 18		
None		
At least one	0.67 (0.50, 0.91)	.01
Perceived health		
SF-12, scale 1-5	0.76 (0.64, 0.90)	< .01
Stress (12 m)		
SECO, scale 1-5	1.51 (1.31, 1.75)	< .01
Psychological consulting		
Never		
At least once	2.54 (1.90, 3.42)	< .01
Mental disorder [b]		
Never		
At least one	4.26 (3.14, 5.80)	<.01
Lifetime drug use		
Alcohol	0.98 (0.55, 1.75)	.95
Tobacco	1.16 (0.85, 1.58)	.37
Cannabis	1.20 (0.89, 1.61)	.22
Cocaine	2.40 (1.51, 3.82)	< .01
MDMA (ecstasy)	1.48 (0.85, 2.56)	.17
Illegal amphetamine	2.44 (1.37, 4.33)	< .01
Ketamine	2.64 (0.88, 7.87)	.08
GHB/GBL	1.54 (0.58, 4.08)	.39

Population-based weights were removed in the regression analyses. [a] ADD/ADHD, narcolepsy, depression, anxiety disorder, dependency (lifetime diagnosis). SF-12: The 12-Item Short Form Health Survey; SECO: State Secretariat for Economic Affairs. N = 10 084. R^2 = .08 (Cox & Snell), .27 (Nagelkerke). Model χ^2 (22) = 648.846, P < .001.

Table 5 Prevalence of nonmedical prescription drug use for PNE in the study population (N = 10 171), main source of supply, and whether the expectations of use were fulfilled.

	LTP	*12-MP*	*30-DP*	*Main source of supply*	*Expectations fulfilled*
Nonmedical prescription drug use					
Tranquilizers	1.06% (108)	0.59% (60)	0.40% (40)	Doctor 53.7% (58)	73.5% (79)
Antidepressants	0.81% (83)	0.37% (38)	0.18% (18)	Doctor 73.8% (61)	70.8% (59)
ADD/ADHD medication	0.57% (58)	0.29% (29)	0.07% (7)	Friend 55.8% (32)	61.0% (35)
Beta-blockers	0.14% (14)	0.04% (4)	0.04% (4)	Doctor 52.8% (8)	72.4% (10)
Modafinil	0.07% (7)	0.04% (4)	0.02% (2)	Friend 31.0% (2)	31.6% (2)
Anti-dementia drugs	0.02% (2)	0	0	Doctor 100.0% (2)	-

Data are % (numbers) adjusted for age, gender, and language region. LTP: lifetime prevalence; 12-MP: 12-month prevalence; 30-DP: 30-day prevalence.

Table 6 Prevalence of PNE motives (M1-M4) among participants who were experienced with alcohol and illegal drug use for a set of multiple-answer options.

	M1. *PCE (attention, concentration, memory)*	***M2.*** *Reduction of nervousness/stage fright*	***M3.*** *PME at work/for studying*	***M4.*** *Relaxation after stress at work/education*
Lifetime drug use				
Alcohol, *n* = 9 541	0.2% (20)	2.4% (233)	0.6% (60)	25.4% (2428)
Cannabis, *n* = 3261	1.0% (33)	2.4% (78)	1.3% (41)	17.4% (568)
Cocaine, *n* = 378	11.6% (44)	2.0% (8)	1.0% (4)	5.7% (22)
MDMA (ecstasy), *n* = 274	3.0% (8)	1.1% (3)	0.3% (1)	6.1% (17)
Illegal amphetamine, *n* = 207	15.2% (31)	2.9% (6)	2.1% (4)	4.5% (9)
GHB/GBL, *n* = 60	0	0	0	2.3% (1)
Ketamine, *n* = 21	5.1% (1)	4.3% (1)	5.1% (1)	0

Data are % (number) adjusted for age, gender, and language region. PCE: pharmacological cognitive enhancement; PME pharmacological mood enhancement.

Figures

Figure 1 Flowchart of the sample composition using the Internet panel of the LINK institute in Switzerland